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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WILDER, CYNTHIA B	
ART UNIT	PAPER NUMBER
1637	

NOTIFICATION DATE	DELIVERY MODE
06/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/584,454	SINGH, SARMAN	
	Examiner	Art Unit	
	CYNTHIA B. WILDER	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The disclosure is objected to because of the following informalities:

(a) The disclosure is objected at pages 10-12 because the designation for the sequence identifier is improper (see MPEP§ 2422.03). It is suggested amending the disclosure to recite --SEQ ID NO:--.

(b) The use of the trademark "Instagene Matrix" at page 15 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate correction is required.

Claim Objections

2. Claims 1-9 are objected to because of the following informalities:

(a) Claims 1, 2 and 9 are objected to because the designation for the sequence identifier (SEQ ID No:) is improper. (see MPEP§ 2422.03). It is suggested amending the disclosure to recite --SEQ ID NO:--.

(a) The article "A" at the beginning of the sequence in the claims 3-8 is improper because the claims refer back to the claim 2. It is suggested amending the claims 3-8 by changing "A" at the beginning of the sentences to --The--.

. Appropriate correction is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1, 2 and 9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter. In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter; *Diamond v. Chakrabaty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims to contain wording such as "Isolated oligonucleotide primer sequences"

5. Claim 10 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 1-10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 1-8 lacks proper antecedent basis for "the banding patterns of amplified fragments" in the claim 1 because the claims do not recite any prior steps wherein banding patterns were obtained. Clarification is required.

(b) Claims 1-8 are indefinite and lacks proper antecedent basis for the recitation of "the target region from the DNA of step (a)" because no target region was identified in the step (a), and it cannot be determined what region Applicant is making reference.

(c) Claims 1- 9 are indefinite and confusing at the recitation of "novel oligonucleotide primers having SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4" in the claims 1, 2 and 9 due to improper claim construction. It cannot be determined if Applicant is suggesting that the different sequences of SEQ ID NOS: 1-4 represent a single combination of primer sequences comprising all 4 sequences or if Applicant intends that the primer sequences be selected from the group consisting of SEQ ID NOS: 1-4 or if Applicant is suggesting something completely different. The claims as currently do not clearly depict Applicant's intent. Clarification is deemed necessary.

(d) Claim 10 is drawn to a method for detecting and differentiating VL and PKDL causing strains of *Leishmania donovani*, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. Appropriate correction is required.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Note: For the purpose of the application of prior art, the claim 10 is being rejected on the same grounds as the claim 2.

9. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Salotra et al (20030162182, August 28, 2003, filing date February 2002) in view of Reed et al (WO 9416331, July 1994) and further in view of Belli et al (Am. J. Trop. Med. Hyg. Vol. 58, no. 1, pages 102-109, 1998). Regarding claims 1-2, 9 and 10, Salotra teach a method, primers and a kit for detecting and differentiating visceral leishmaniasis (VL, also called kala-azar, KA) and post Kal-azar dermal leishmaniasis (PKDL) causing o *Leishmania donovani* in a sample, the method comprising the steps of (a) isolating DNA from a sample; (b) amplifying a target region from the DNA of step (a) using isolated primer sequences and heat stable DNA polymerase to obtain amplified fragments, (c) separating the amplified fragments of step (b); and (d) analyzing the fragment of step (c) to detect and differentiate VL and PKDL causing strains of Leishmania donovani based on a banding pattern of the amplified fragments following electrophoresis (0025-0031 and 0038, see also Table 1 which gives results of PCR assay in KA and PKDL clinical samples and control; see also 0034 which teaches the concept of a kit comprising reagents for performing the method. It is noted that the presence of an instruction

manual is deemed inherent in the kit. Further MPEP states, "Where the only difference between a prior art product and a claimed product is printed matter that is not functionally related to the product, the content of the printed matter will not distinguish the claimed product from the prior art. *In re Ngai*, >367 F.3d 1336,1339, 70 USPQ2d 1862, 1864 (Fed. Cir. 2004))".

Regarding claim 3, Salotra et al teach wherein the sample is a clinical sample or culture sample (0032, 0037, 0038 and Table 1).

Regarding claim 4, Salotra et al teach wherein the clinical sample is selected from the group consisting of blood, skin, or bone marrow aspirates (see 0032, 0037, 0038 and Table 1).

Regarding claim 5, Salotra et al teach wherein the step (b) the heat stable DNA polymerase is Taw polymerase (0028).

Regarding claim 6, Salotra et al teach wherein in step (b) the amplification is done by polymerase chain reaction (PCR) (0029).

Regarding claim 7, Salotra et al teach wherein in the step (c) separation is done preferably by gel electrophoresis (0030).

Regarding claim 8, Salotra et al teach wherein the step (d) of the detection is by ethidium bromide (0045).

Salotra et al differs from the instant invention in that the reference does not teach the primer sequences of SEQ ID NOS: 1-4 or wherein the primers are all used in a single polymerase chain reaction.

Reed et al teach a nucleic acid sequence of Leishmania comprising a sequence substantially identical to the sequence of *SEQ ID NO: 1* (see page 17, SEQ ID NO: 2 which teaches a sequence 100% identical to SEQ ID NO: 1 at nucleotide position 2681 to 2697) (see alignment below);

```
SEQ ID NO: 1          1 CTAGAGCAGCAGCTTCG 17
                        |||||||||||||||||
Reed et al         2681 CTAGAGCAGCAGCTTCG 2697
SEQ ID NO: 2
```

SEQ ID NO: 2 (see page 17, SEQ ID NO: 2 which teaches a sequence 100% identical to the sequence of SEQ ID NO: 2 at nucleotide position 2564 to 2580) (see alignment below);

```
SEQ ID NO: 2          1 CTTGAGCAGCAGCTTCG 17
                        |||||||||||||||||
Reed et al         2564 CTTGAGCAGCAGCTTCG 2580
SEQ ID NO: 2
```

SEQ ID NO: 3 (see page 17, SEQ ID NO: 2 which teaches a complement sequence that is 100% identical to the sequence of SEQ ID NO: 3 at nucleotide positions 2797 to 2781) (see alignment below);

```
SEQ ID NO: 3          1 CGTGGCCCTCGTGTTCT 17
                        |||||||||||||||||
Reed et al         2797 CGTGGCCCTCGTGTTCT 2781
SEQ ID NO: 2
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and SEQ ID NO: 4 (see page 17, SEQ ID NO: 2 which teaches a complement sequence 82. 4% identical to the sequence of SEQ ID NO: 4 at nucleotide positions 3265 to 3252) (see alignment below).

```
SEQ ID NO: 4          1 CGCGGCCCTCGTGT 14
                        ||||||||||||||
Reed et al         3265 CGCGGCCCTCGTGT 3252
SEQ ID NO: 2
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In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated, "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound... Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs of the DNA sequence as taught Reed et al and which are derived from sequences expressly suggested by the prior art and known in the prior art for the detection of Leishmaniasis and concerning which a biochemist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers and probes are *prima facie* obvious over the cited references in the absence of secondary considerations.

Salotra et al in view of Reed et al do not expressly teach wherein multiple primers are used in the same PCR assay. However, multiplex PCR using multiple primer sequences is well known and commonly applied in biochemical studies. For example, Belli et al teach a multiplex PCR reaction using multiple primers that allows simultaneous detection of the Leishmania genus (abstract and page 103, section

entitled "Polymerase chain reaction amplification"). Belli et al teach that the multiplex reaction minimizes the number of PCRs necessary to characterize the Leishmania strains (see page 4, col. 2, last paragraph). Belli et al teaches that PCR offers certain advantages over classic techniques for diagnosis and characterization of infectious pathogens. Belli et al teach when appropriately applied, the PCR can be more specific, sensitive, versatile, and rapid than conventional methods; in addition, genetic information can be obtained in the process (last paragraph, col. 2, page 106). Belli et al teaches that PCR is particularly useful in case of leishmaniasis, due to the requirement for parasitologic confirmation and to the limitations of classic methodologies (page 107, col. 1, second paragraph).

In would have been *prima facie* obvious for one of ordinary skill in the art at the time of the claimed invention to have been motivated to have modified the amplification reaction of Salotra et al in view of Reed et al to encompass a PCR reaction comprising the use of multiple primers in a multiplex reaction as taught by Belli et al. One of ordinary skill in the art at the time of the claimed invention would have been motivated to do for the advantages of reducing the number of PCRs necessary to characterize Leishmania strains as suggested by Belli et al. One of ordinary skill in the art would have been further motivated to use the PCR reactions as taught by Belli for the additional advantages of increase specificity, sensitivity and versatility as taught by Belli.

Conclusion

10. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
Examiner, Art Unit 1637